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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,878	10/31/2003	Takashi Komai	2003-1593A	9005

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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/697,878	KOMAI ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/30/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election of the claims of Group I corresponding to claims 1-10 in the reply filed on 11/06/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL. Claims 11-12 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected subject matter.

An action on the merits of claims 1-10 is contained herein below.

35 U.S.C. 112, first paragraph rejection

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 8 and 9 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the anti-coagulant polysaccharide sulfated gellan (GS) useful for treatment of myocardial infarction, cerebral infarction or venous thrombosis does not reasonably provide enablement for the anti-coagulant polysaccharide sulfated gellan useful for the prevention of myocardial infarction, cerebral infarction or venous thrombosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors regarding undue experimentation have been summarized in *In re Wands,* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

(1) The quantity of experimentation necessary (time and expense);

(2) The amount of direction or guidance presented;

(3) The presence or absence of working examples of the invention;

(4) The nature of the invention;

(5) The state of the prior art;

(6) The predictability or unpredictability of the art;

(7) The breadth of the claims; and

(8) The relative skill of those in the art.

Breath of claims

The instant claims are drawn to the anti-coagulant polysaccharide sulfated gellan (GS) useful for the prevention and treatment of myocardial infarction, cerebral infarction or venous thrombosis. One of ordinary skill in the art would not be apprised of the metes

and bounds of GS useful in the prevention of myocardial infarction, cerebral infarction or venous thrombosis.

Nature of Invention

The invention relates to GS as an anti-coagulant agent, an anti-thrombus agent or a blood contact face-treating agent for medical equipment.

State of the Prior Art

Yamamoto et al. (cited in IDS, 2003) is representative of the prior art at the time of the invention. Yamamoto et al teach that GS in combination with chitosan can be used as a biomedical selective artificial ligand for use in removing a complex of extra domain A containing fibronection from plasma in rheumatoid arthritis patients (page 2053, 1st para.). While some progress has been made, myocardial infarction, cerebral infarction or venous thrombosis is still among the diseases most difficult to treat. Despite growing understanding of diseases related to thrombosis along with improved techniques for detecting and treating them, few anti-thrombus drugs have proved effective. Further, new thrombus related diseases constantly appear as an inevitable consequence of evolution. Thus, searching for a novel and effective way of preventing the myocardial infarction, cerebral infarction or venous thrombosis remains imperative and challenging. In developing an anti-thrombus agent, it is well known that inhibitory activity of an ant-thrombus agent against a particular thrombosis cannot be equated with its inhibitory effect against another thrombosis. For example, heparin has proved to be specifically effective against certain thrombosis related diseases not against all possible thrombosis, even both heparin and GS belong to the same sulfated polysaccharide

family. Without the knowledge of a thrombosis's genetic traits and the chemical properties of an ant-thrombus agent, prevention of a thrombosis related disease becomes unpredictable.

Level of Ordinary Skill in the Art

The level of ordinary skill in the art is seen to be a M.D. experienced in the prevention of myocardial infarction, cerebral infarction or venous thrombosis or a Ph.D in the field of biomedical research.

Level of Predictability in the Art/Amount of Direction Provided by the Inventor

Please note that a single embodiment may provide broad enablement in cases involving predictable factors, but more is required in cases involving unpredictable factors, such as chemical or physiological activity, see *Ex. Parte Hitzeman,* 9 USPQ2d 1821. In the instant case, no experimental data or citations of relevant prior art are presented in support of applicant's assertion that the prevention of myocardial infarction, cerebral infarction or venous thrombosis is accomplished by administering a patient GS as an anti-thrombus agent. The prior art (Yamamoto; as discussed above) discloses that without the knowledge of a thrombosis's genetic traits and the chemical properties of an anti-thrombus agent agent, prevention of myocardial infarction, cerebral infarction or venous thrombosis becomes unpredictable. Additionally, the instant specification provides no guidance as to how the skilled artisan would address various factors of administration of GS as an anti-thrombus agent.

Working Examples

The working examples 1-4 discloses a method for sulfation of gellan and their use to measure the coagulation time of the normal blood.

Quantity of Experimentaion Needed to make and/or use the Invention Based on the Content of the Disclosure

When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation. In the instant case, the phrase "for prevention" limits the composition/kit. There are no teachings in the prior art suggesting the broad prevention of the diseases related to thrombosis using a single composition of particular treatment regimen. Applicant has not provided any working examples. As such, a skilled artisan would not recognize that an anti-thrombus agent GS is useful in the prevention of myocardial infarction, cerebral infarction or venous thrombosis as broadly claimed.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(1) The phrase "capable of" in claim 8, is a relative term, which renders the claim indefinite. The pharse "capable of" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(2) Claims 8 and 9 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claims 1-6. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyamoto et al. (International Journal of Biological Macromolecules, 2001; cited in IDS).

The applicants' claims are directed toward a polysaccharide which is modified by sulfation from 8-80%; the polysaccharide is gellan and modified polysaccharide is gellan sulfate (GS).

Miyamoto et al. disclose the preparation of GS from gellan wherein the hydroxyl groups are sulfated (page 382, 1st col., 2.2). The reference does not indicate that the degree of sulfation is between 8-80% however the results are shown where the degree of sulfation is upto 40% (page 383, Fig.3). It is inherent property of a gellan polysaccharide to

undergo sulfation upto 100% in a sulfation reaction through its available hydroxyl groups. Furthermore, it is well known in the art that the constituent sugars of gellan are glucose, glucuronic acid and rhamnose in the molar ratio of 2:1:1. Miyamoto et al. also disclose the Formula (I) of claim 2 (page 383, Fig.2). Therefore Miyamoto et al's GS is encompassed by the applicants' claims.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

Claims 5-10 are rejected under 35 U.S.C. 103(a) as being obvious over Miyamoto et al. (International Journal of Biological Macromolecules, 2001; cited in IDS).

It is noted that the anti-thrombus agent useful for medical equipment; the prevention and treatment of myocardial infarction, cerebral infarction or venous thrombosis; and their processing is claimed in the preamble of claims 8-10. In a compound/composition claim, the intended use or the process of the compound/composition does not have any patentable weight towards the claimed compound/composition.

Miyamoto et al. teach the preparation of GS from gellan wherein the hydroxyl groups are sulfated (page 382, 1st col., 2.2). Miyamoto et al teach that GS can be used

as a biomedical selective artificial ligand for use in removing a complex of extra domain A containing fibronection (FN) from plasma in rheumatoid arthritis patients because the high selectivity of GS property for EDA(+)FN as an artificial ligand probably depends on the saccharide conformation, sulfuric groups density and position of gellan that closely relates with the sulfuric and carboxyl groups (page 384, last para.). The reference does not indicate that the degree of sulfation is between 8-80% however the results are shown where the degree of sulfation is upto 40% (page 383, Fig.3). It is inherent property of a gellan polysaccharide to undergo sulfation upto 100% in a sulfation reaction through its available hydroxyl groups. Furthermore, it is well known in the art that the constituent sugars of gellan are glucose, glucuronic acid and rhamnose in the molar ratio of 2:1:1. Miyamoto et al. also disclose the Formula (I) of claim 2 (page 383, Fig.2). With regard to the very broad ranges of mean molecular weight of the sulfated polysaccharide between 1 to 1000 or 1 to 30 KDa of claims 5 and 6, Miyamoto et al's GS discloses the average unit number (n) of gellan between 50-100 (page 383, Fig.2), it would be within the scope of the artisan in this art to optimize them through routine experimentation in the absence of unexpected results with a particular combination. Miyamoto et al. also discloses the solubility of GS in buffer medium in the study of their affinity constant (page 382, 2nd col.), it would be within the scope of the artisan in this art to optimize the GS preparation in a buffer suitable for intravenous administration, intestinal administration or oral administration through routine experimentation. It is noted that GS is structurally close to an anti-thrombus agent heparin because in both of these polysaccharide the hydroxyl groups are partially sulfated therefore GS can also

be used as an anti-thrombus agent due to inherent properties of the sulfated polysaccharide.

It would have been obvious to person having ordinary skill in the art at the time the invention was made, to modify gellan polysaccharide because the hydroxyl group can be easily modified by chemically targeting the sulfate group to use in the pharmaceutical compositions as taught by Miyamoto et al's reference. The motivation is provided by Miyamoto et al., the prior art suggests that GS can be used as a biomedical selective artificial ligand for use in removing a complex of extra domain A containing fibronection (FN) from plasma in rheumatoid arthritis patients because the high selectivity of GS property for EDA(+)FN as an artificial ligand probably depends on the saccharide conformation, sulfuric groups density and position of gellan that closely relates with the sulfuric and carboxyl groups (page 384, last para.).

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at

(571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Devesh Khare, Ph.D.,J.D.
Art Unit 1623

February 2, 2007